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10/708,432	03/03/2004	Thomas Plummer	ACIZ-148-101	2431

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HELM, CARALYNNE E	
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02/18/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/708,432	PLUMMER ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7-10,12,13 and 15-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,7-10,12,13 and 15-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/9/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

MAINTAINED REJECTIONS

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquiries of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-5, 7, 10, 13, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phipps (previously cited) in view of the Table of pKa and PI values for amino acids (previously cited) and Petelenz et al. (previously cited).

Phipps teaches an electrotransport device where the pH of the reservoirs is optimized to reduce skin irritation both before and after electrotransport drug delivery (see column 3 lines 60-64). In addition, Phipps teaches that iontophoresis is a widely used process of electrotransport. Phipps generally teaches that these devices have one electrode that is termed a donor or active electrode while the other is the counter or return electrode, serving to close the circuit through the body (see column 1 lines 43-47; instant claim 4). One embodiment of the device is configured where an electrical power source is connected to the donor (active) electrode, which includes the donor reservoir with the drug to be delivered (see column 5 lines 34-39; instant claims 1 and 4). The invention of Phipps is envisioned using a variety of electrode configurations including one where the power source and electrodes are not a unitary device. In particular, Phipps points to the teachings of Petelenz et al. as one such alternative. Phipps goes on to further describe the donor and counter reservoirs used in the invention. Both are taught as polymeric gel matrices that can include polymers in combination such as Klucel®, a hydroxypropyl cellulose and a viscosity enhancer also exemplified by the instant application, as well as hydroxyethyl cellulose (see column 17 lines 10-13 and 26,

and 32-33; instant claims 1, 7, and 14 and instant specification paragraph 17 line 14-16). WATER LOCK®, a sodium polyacrylate polymer, is also taught in this group of suitable polymers and is also taught as a rehydrating agent in the instant specification (see column 17 lines 24-25; instant specification paragraph 17 lines 17-19; instant claim 15). Polymeric buffers are taught by Phipps for use in an anodic reservoir to eliminate competition between the drug to be delivered and the counter ions that can be produced by some buffers (see column 15 lines 7-17). In particular, poly(methylvinyl ether-maleic acid), sold commercially as Gantrez® S95 and S97, is given as a particularly envisioned example of such a polymeric buffer, and is also exemplified in the instant specification (see table 7; instant claim 5 and specification paragraph 15). As the anodic reservoir is taught to be maintained at pH 4 or greater (interpreted as about 4.5), its exemplified buffers are capable of performing this function (see column 15 lines 59-65; instant claims 1, 10, and 16). It is also taught that the combination of anionic and cationic buffers can be used where amino acids are particularly envisioned in either role (see column 14 lines 25-27). The buffering agents are taught used at about 0.01M to about 1.0M (see column 8 lines 18-19). "About 1.0M" is interpreted to include values above 1.0M which thereby meet applicants' requirement of greater than about 1.0M, which can be interpreted as 1.0M (see instant claims 1 and 10). Phipps goes on to discuss the classifications of drugs (medicaments) that can be delivered by the invention (see column 18 line 43-column 19 line 45). An example teaches a polyvinyl alcohol based hydrogel that contains lidocaine HCl (medicament) and is used to deliver the drug to a living patient through the skin; here, the potassium concentration is monitored as an

indicia of skin irritation and to indicate the need to reposition the device (see example 7). The teachings of Phipps do not explicitly describe the combination of acidic polymeric buffer and a basic amino acid; however, the range over which poly(methylvinyl ether-maleic acid) buffers is nearly the same as that of the acids exemplified. Thus this polymer can be classified as an acidic polymeric buffer. In addition, since both amino acids and polymeric buffers are taught to be available in cationic or anionic form, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine a polymeric buffer with an amino acid buffer.

Phipps refers to figure 6 of Petelenz et al. as a teaching of iontophoretic device configurations that are contemplated within the invention. Figures 5 and 6 depict an electrode assembly where a first electrode is in electrical communication with the medicament in the medicament medium (polymeric matrix) and a second electrode is remote from the first and in contact with the patient's body (see column 13 lines 26-44; instant claims 1 and 10). There is no recited requirement that there be any material separating the remote electrode from the subject's skin. Thus, it would have been obvious to one of ordinary skill that the connection between the electrode and the subject's body would be direct physical, and therefore also electrical, communication.

Glycine (exemplified by applicant's disclosure) is not specifically taught by Phipps as a basic amino acid suitable for use in the invention, however the pKa of its ammonium ion is near that of histidine (see Table of pKa and PI values for amino acids), which is included in the list taught by Phipps. Since the pKa of a compound

controls its ability to buffer, the closeness of glycine's value (9.6) to histidine's value (9.17) makes them equivalents for the purposes of the invention of Phipps.

Based upon these teachings, the combination of polymeric buffers with amino acids would have been a known option within the technical grasp of one of ordinary skill in view of the teachings of Phipps. Since both glycine and histidine are included in the twenty most common amino acids, the exchange of one for another for the same purpose would have been obvious to one of ordinary skill (see instant claims 13 and 16). Further, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for the combination of an amino acid with a polymeric buffer as an appropriate buffering system in the invention of Phipps and achieve the instantly claimed invention (anionic polymeric buffer with cationic amino acid). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make and use the invention of Phipps where the polymeric gel matrix includes a polymeric and amino acid buffering system (maintaining the pH at about 4.5), viscosity enhancer, rehydrating agent and medicament with an electrode assembly configured as taught by Petelenz et al. for iontophoretic delivery of the medicament to a living subject's body. In this configuration the polymeric gel and its associated components would be the medicament medium in contact with electrode 12 as depicted in figure 5 of Petelenz et al. Therefore, claims 1, 4-5, 7, 10, 13, and 16 are obvious over Phipps in view of the Table of pKa and PI values for amino acids and Petelenz et al.

Claims 1, 3, 10, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phipps in view of the Table of pKa and PI values for amino acids and Petelenz et al. as applied to claims 1, 4-5, 7, 10, 13, and 16 above, and further in view of the lidocaine record in the Merck Index.

The modified Phipps reference makes obvious the recitations of instant claims 1 and 10. Phipps also teaches the incorporation of several classes of drugs (medicaments) that includes anesthetic (see column 18 lines 43-45 and 53-54) In a particular example, Phipps teaches the delivery of the anesthetic lidocaine HCl, a derivative of lidocaine commonly used in the art (see Phipps-example 7 and Lidocaine - Merck Index). As the HCl derivative of lidocaine is commonly used for lidocaine in the pharmaceutical art, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use lidocaine as the medicament in the invention of Phipps. Thus, claims 1, 3, 10, and 12 are obvious over Phipps in view of the Table of pKa and PI values for amino acid, Petelenz et al., and the Merck Index.

Claims 1, 3, 9-10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phipps in view of the Table of pKa and PI values for amino acids and Petelenz et al. as applied to claims 1, 4-5, 7, 10, 13, and 16 above, and further in view of Parkinson et al. (previously cited).

The modified Phipps reference makes obvious the recitations of instant claims 1 and 10. Phipps also teaches the incorporation of several classes of drugs (medicaments) that includes anti-inflammatory compounds (see column 18 lines 43-45 and 56). Phipps does not teach the particular type of anti-inflammatory compound or the

particular type of active electrode assembly to employ for the donor electrode to use in the invention.

Parkinson et al. teach an iontophoretic device for delivery of anti-inflammatory steroids that includes water-soluble forms of dexamethasone in particular (see paragraph 4 lines 1-21, paragraph 16 and paragraph 17). Parkinson et al. also teach that in an iontophoretic device the active electrode assemblies can be open faced as well as high-density electrodes (see paragraph 16 and paragraph 37 lines 11-13). Since it was know to deliver dexamethasone iontophoretically and the device of Phipps allows this mechanism of delivery with less skin irritation, it would have therefore been obvious to one of ordinary skill in the art to use dexamethasone in the polymeric gel reservoir matrix in the invention of Phipps in view of the Table of pKa and PI values for amino acids and Petelenz et al. It further would have been obvious to select an open faced or high-density electrodes as the active electrode assembly in this invention since these were particular varieties of electrodes known for use in such devices. Therefore claims 1, 3, 9-10, and 12 are obvious over Phipps in view of the Table of pKa and PI values for amino acid, Petelenz et al., and Parkinson et al.

Claims 10 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phipps in view of the Table of pKa and PI values for amino acids and Petelenz et al. as applied to claims 1, 4-5, 7, 10, 13, and 16 above, and further in view of the Grain Processing Corporation WATER LOCK Superabsorbent Polymers reference.

The modified Phipps reference makes obvious the recitations of instant claim 10. In a particular embodiment, Phipps teaches a polyvinyl alcohol (polymer gel matrix) with hydroxypropylmethylcellulose (viscosity enhancer and rehydrating agent) (see column 26 lines 54-58). Phipps also teaches other polymers such as KLUCEL® and WATER LOCK®, that are useful both individually and in combination, as components in the electrode reservoirs (see column 17 lines 10-13 and 26, and 32-33; instant specification paragraph 17 line 14-16). Phipps does not teach a particular variety of WATER LOCK®, but instead implies that any would be suitable. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ WATER LOCK® A220, as a finite number of variants were available and all served the purpose of absorbing water at the time of the invention (see the Grain Processing Corporation WATER LOCK® Superabsorbent Polymers reference). Therefore claims 10 and 15 are obvious over Phipps in view of the Table of pKa and PI values for amino acids, Petelenz et al., and the Grain Processing Corporation WATER LOCK® Superabsorbent Polymers reference.

NEW REJECTIONS

Claim Objections

Claim 20 is objected to because of the following informalities: the recitation of "a polymer having pendant carboxylic acid moieties and an amino acid" is unclear as to whether this is an amino acid and a polymer having pendant carboxylic acid moieties or

a polymer having both pendant carboxylic acid moieties and an amino acid in its structure. Appropriate correction is required.

For the sake of application of prior art, this recitation is interpreted as an amino acid and a polymer having pendant carboxylic acid moieties.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-5, 7-10, 12-13, and 15-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1, 10, and 19 recite “the buffering agent…is present in a concentration greater than about 1.0M”. This recitation has no basis in the disclosure as filed since the molarity of the buffering agent was not discussed and none of the weight percentage concentrations that are discussed correspond to 1.0M. Thus this recitation is new matter. Claims 3-5, 7-9, 12-13, and 15-16 are rejected as well since they depend from claims 1 and 10. In addition claims 17 and 21-22 recite "sodium polyacrylate having a concentration of less than about 0.6% by weight.” This recitation also does not have basis in the disclosure since this number is not associated with the sodium polyacrylate.

Claim Rejections - 35 USC § 103

Claims 1, 8, 10, and 17-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phipps in view of the Table of pKa and PI values for amino acids and Petelenz et al. as applied to claims 1, 4-5, 7, 10, 13, and 16 above, and further in view of Hsu et al. (previously cited).

The modified Phipps reference makes obvious the recitations of instant claims 1 and 10 as well as a two electrode assembly for the device and both the variety and concentration of buffering agents, as claimed (see instant claims 18-20). In addition, Phipps teaches sodium polyacrylate and hydroxylethyl cellulose present at any proportion in the composition, where both low and higher proportions are envisioned (see column 17 lines 10-15; instant claim 21-22). Phipps also teaches the incorporation of additional ingredients in the reservoir matrix such as permeability enhancers, but does not teach particular examples of chemicals that could serve in this role.

Hsu et al. teach that a variety of compounds are used in the art of drug delivery to enhance skin permeability that includes polysorbate 20 (TWEEN® 20) (see paragraph 5 lines 1-3 and 11; instant claims 8 and 17). It would have therefore been obvious to one of ordinary skill in the art to use polysorbate 20 as a permeability enhancer in the polymeric gel matrix to aid in drug delivery in the invention of Phipps in view of the Table of pKa and PI values for amino acids and Petelenz et al. Thus claims 1, 8, 10, and 17-22 are obvious over Phipps in view of the Table of pKa and PI values for amino acids, Petelenz et al., and Hsu et al.

Response to Arguments

Applicants' arguments filed November 9, 2009 have been fully considered but they are not persuasive.

Applicants' argue against the combination Petelenz and Phipps; however the citation of Petelenz et al. is only in the context in which it is cited within Phipps. The Phipps reference refers to the electrode configurations in Petelenz as examples of those that are suitable for their taught iontophoretic devices, but do not describe this configuration further. For this reason and this reason only, Petelenz et al. is cited to provide the description of the electrode configuration that was envisioned by Phipps. Additionally as discussed above, Phipps does make obvious including a buffering agent at 1.0M or greater as well as maintaining the gel matrix pH from approximately 4.1 to approximately 4.9 in an iontophoretic device.

Applicants go on to argue that the teachings of Phipps combined with Hsu et al. does not teach the classification of polysorbate 20, sodium polyacrylate or hydroxyl ethyl cellulose as rehydrating agents or viscosity enhancers. As applicants are free to be their own lexicographer, classifying ingredients as they choose, other authors also have this freedom; however neither style of classification changes the ingredients themselves. "A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present." This treatment results from In re Spada, which states that, "Products of identical chemical composition can not have mutually exclusive properties." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) (see MPEP 2112.01). Since Phipps in view of Hsu et al. teach polysorbate 20, sodium polyacrylate, and hydroxyl ethyl

cellulose, as taught by applicants, these components must have the properties that are claimed (e.g. viscosity enhancement or rehydration agent) because they are the same chemical compounds. Finally applicants argue that the teaching of a few percent to 50 percent of hydrophilic polymers, that can include both sodium polyacrylate and hydroxyl ethyl cellulose, does not suggest sodium polyacrylate at less than 0.6% and hydroxyl ethyl cellulose at less than 0.3%, each by weight. While there is not an explicit teaching of these precise proportions, the teachings of Phipps of these components being used at any ratio relative to the other components in the matrix gives one of ordinary skill in the art ample room for routine experimentation that would render obvious the claimed concentrations (see column 17 lines 10-14).

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The rejections and/or objections detailed above are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615